

7. (Amended) A method according to claim 1 wherein said set of primary variant amino sequences optimized for at least one scoring function comprises the globally optimal protein sequence.

C2 8. (Amended) A method according to claim 1 wherein said scoring function is selected from the group consisting of a van der Waals potential scoring function, a hydrogen bond potential scoring function, an atomic salvation scoring function, an electrostatic scoring function and a secondary structure propensity scoring function.

Please cancel Claim 6 without prejudice or disclaimer.

#### REMARKS

Claims 1-17 are pending in this application. Claim 1 has been amended to clarify the claim language. Support for this amendment may be found in the Specification at page 5, lines 1-6 and page 24, lines 29-34 and original Claim 6. Claim 6 has been canceled by this Response. Claims 7 and 8 have been amended to depend from amended Claim 1. Applicants submit that no new matter has been added by this amendment.

#### Claim Rejection 35 USC §112, Second Paragraph

Claim 1-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention.

A. The Office Action states that the claims vague and indefinite because they are drawn to an *in silico* method of modulating protein immunogenicity, a biological function that may only be determined experimentally. The present invention is directed to a method for modulating immunogenicity by inputting a protein backbone structure with variable residue positions into a computer, computationally generating a set of primary variant amino acid sequences and applying a computational immunogenicity filter against said set to identify at least one candidate variant protein. Applicants submit that the Examiner correctly states in the present Office Action that "computerized methods of generating peptide libraries with substitutions at variable positions proved to be an efficient way of modeling peptides which are further assessed for their biological functions." See page 7 of the present Action, citing Mayo et al. WO 98/47089 and US Patent No. 6,269,312. Applicants further submit that additionally applying the computational immunogenicity filter, results in variant sequences having modulated immunogenicity.